CLAIMS

What Is Claimed Is:

SUB A3

1. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein, or fragment, analog or variant thereof, to model a BPI protein.

2. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein, or fragment, analog or variant thereof, to model a BPI-related lipid transfer protein.

3. The use according to claim 2, wherein the BPI-related lipid transfer protein is lipopolysaccharide-binding protein (LBP), cholesteryl ester transferase protein (CETP) or phospholipid transfer protein (PLTP), or fragment, analog or variant thereof.

4. The use according to any of claims 1-3, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 31.

5. The use according to any of claims 1-3, wherein the BPI protein comprises a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.

6. The use according to any of claims 1-3, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 3 and a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.

7. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein to computationally design a chemical compound for mimicking BPI protein, or fragment, analog or variant thereof.

8. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein to computationally design a chemical compound for mimicking a BPI-related lipid transfer protein, or fragment, analog or variant thereof.

9. The use according to claim 8, wherein the BPI-related lipid transfer protein is lipopolysaccharide-binding protein (LBP), cholesteryl ester transferase protein (CETP) or phospholipid transfer protein (PLTP).

10. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein, to design a chemical compound capable of associating with a BPI-related lipid binding protein, or fragment, analog or variant thereof.

11. The use according to claim 10, wherein the BPI-related lipid binding protein is lipopolysaccharide-binding protein (LBP), cholesteryl ester transferase protein (CETP) or phospholipid transfer protein (PLTP), or fragment, analog or variant thereof.

12. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein to design a model of ligands in an active site of a lipid binding protein.

13. The use according to claim 12, wherein the lipid binding protein is bactericidal/permeability-increasing protein (BPI), lipopolysaccharide-binding protein (LBP), cholesteryl ester transferase protein (CETP) or phospholipid transfer protein (PLTP), or fragment, analog or variant thereof.

14. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein, to design compounds with at least one activity selected from the group consisting of antibacterial, antifungal, antimycobacterial, antichlamydial, antiprotozoan, heparin-binding, endotoxin-binding, heparin-neutralizing, endotoxin-neutralizing, inhibition of tumor and

endothelial cell proliferation, inhibition of angiogenesis, anti-inflammatory, anticoagulant and antithrombolytic.

15. The use according to any of claims 1 - 14, wherein said atomic coordinates are according to Table 4.

16. A method of three-dimensional modeling of a bactericidal/permeability-increasing ("BPI") protein comprising the steps of:

(a) providing three-dimensional atomic coordinates derived from X-ray diffraction measurements of a BPI protein in a computer readable format;

(b) inputting the data from step (a) into a computer with appropriate software programs;

(c) generating a three-dimensional structural representation of the BPI protein suitable for visualization and further computational manipulation.

17. A method of three-dimensional modeling of a bactericidal/permeability-increasing ("BPI")-related lipid transfer protein comprising the steps of:

(a) providing three-dimensional atomic coordinates derived from X-ray diffraction measurements of a BPI protein in a computer readable format;

(b) inputting the data from step (a) into a computer with appropriate software programs;

(c) generating a three-dimensional structural representation of the BPI-related lipid transfer protein suitable for visualization and further computational manipulation.

18. The use according to any of claims 16-17, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 3.

19. The use according to any of claims 16-17, wherein the BPI protein comprises a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about

65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.

20. The use according to any of claims 16-17, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 3 and a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.

21. A method for providing an atomic model of a BPI protein, or fragment, analog or variant thereof, comprising

(a) providing a computer readable medium having stored thereon atomic coordinate/x-ray diffraction data of the BPI protein, or fragment, analog or variant thereof, in crystalline form, the data sufficient to model the three-dimensional structure of the BPI protein, or fragment, analog or variant thereof;

(b) analyzing, on a computer using at least one subroutine executed in said computer, atomic coordinate/x-ray diffraction data from (a) to provide atomic coordinate data output defining an atomic model of said BPI protein, or fragment, analog or variant thereof, said analyzing utilizing at least one computing algorithm selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

(c) obtaining atomic coordinate data defining the three-dimensional structure of at least one of said BPI protein, or fragment, analog or variant thereof.

22. A method according to claim 21, wherein said computer readable medium further has stored thereon data corresponding to a nucleic acid sequence or an amino acid sequence data comprising at least one structural domain or functional domain of a BPI, LBP, CETP or PLTP corresponding to at least one BPI or mutant primary sequence of Figures 2-20 or Table 2, or a fragment thereof; and wherein said analyzing step further comprises analyzing said sequence data.

23. A computer-based system for providing atomic model data of the three-dimensional structure of BPI protein, or fragment, analog or variant thereof, a BPI mutant or a BPI fragment, comprising the following elements:

(a) at least one computer readable medium (CRM) having stored thereon atomic coordinate/x-ray diffraction data of said BPI protein, or fragment, analog or variant thereof;

(b) at least one computing subroutine that, when executed in a computer, causes the computer to analyze atomic coordinate/x-ray diffraction data from (a) to provide atomic coordinate data output defining an atomic model of said BPI protein, or fragment, analog or variant thereof, said analyzing utilizing at least one computing subroutine selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

(c) retrieval means for obtaining atomic coordinate output data substantially defining the three-dimensional structure of said BPI protein, or fragment, analog or variant thereof.

24. A method for providing a computer atomic model of a ligand of a BPI protein, or fragment, analog or variant thereof, comprising

(a) providing a computer readable medium (CRM) having stored thereon atomic coordinate data of a BPI protein, or fragment, analog, or variant thereof;

(b) providing a CRM having stored thereon atomic coordinate data sufficient to generate atomic models of potential ligands of said BPI protein, or fragment, analog, or variant thereof;

(c) analyzing on a computer, using at least one subroutine executed in said computer, the atomic coordinate data from (a) and ligand data from (b), to determine binding sites of BPI protein, or fragment, analog, or variant thereof, and to provide atomic coordinate data defining an atomic model of at least one ligand of said BPI, BPI mutant or a fragment thereof, said analyzing utilizing computing subroutines selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

(d) obtaining atomic coordinate model output data defining the three-dimensional structure of said at least one ligand of said BPI protein, or fragment, analog, or variant thereof.

25. A computer-based system for providing an atomic model of at least one ligand of a BPI, BPI mutant or a fragment thereof, comprising the following elements;

(a) a computer readable medium (CRM) having stored thereon atomic coordinate data of a BPI, mutant or fragment thereof;

(b) a CRM having stored thereon atomic coordinate data sufficient to generate atomic models of potential ligands of a BPI, mutant or fragment;

(c) at least one computing subroutine for analyzing on a computer, the atomic coordinate data from (a) and (b), to determine binding sites of BPI protein, or fragment, analog, or variant thereof, and to provide

data output defining an atomic model of at least one potential ligand of BPI protein, or fragment, analog, or variant thereof, said analyzing utilizing at least one computing subroutine selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

(d) retrieval means for obtaining atomic coordinate data of said at least one ligand of a BPI protein, or fragment, analog or variant thereof.